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SYNTHETIC ORGANIC CHEMICALS

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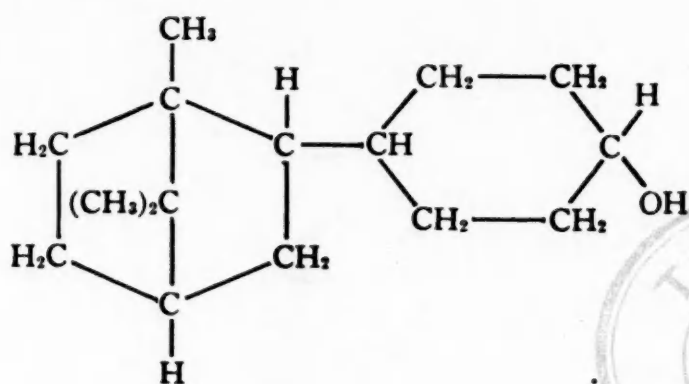
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New Woody-Type Odors of Interest to the Perfume Industry*

By JOHN R. BYERS, JR.**

SEVERAL interesting and important additions to the perfume industry have been disclosed recently in the vast amount of chemical and other technical data collected by the U. S. Army Intelligence in Germany. Among these are two new groups of aliphatic alcohols which are valuable because of the fidelity with which they reproduce the fragrance of the oils of sandalwood and vetiver.

One group of these alcohols consists of a series of alkyl-substituted cyclohexanols. The lowest member of the series is 4-camphylcyclohexanol which probably has the structure

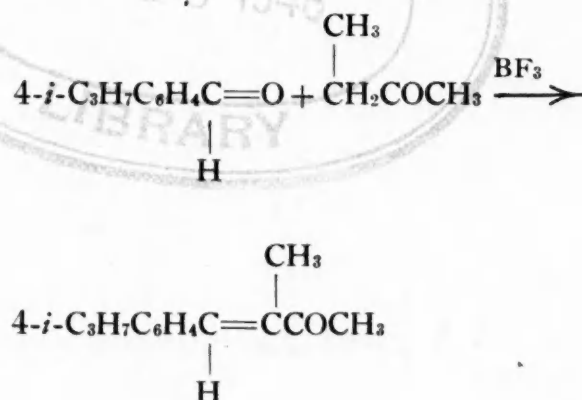


It seems likely that this substance can be made cheaply by starting with borneol and phenol. Borneol reacts with phenol at the para-position in the presence of acidic reagents such as *p*-toluene-

sulfonic acid or aluminum chloride. It is then necessary to hydrogenate the benzene ring of the product in order to obtain the fragrant cyclohexanol derivative. Analogs are obtained by the use of substituted phenols. These products actually have the true woody sandalwood fragrance. It should be interesting to note the effect on the fragrance of substituent groups on both the camphyl and the phenol rings.

The second group of alcohols is important not only because the individual members have odors of the sandalwood and vetiver types, but also because in their preparation a seldom-used type of aldol condensation is employed. This reaction is brought about by acidic catalysts such as boron trifluoride or the active earths.

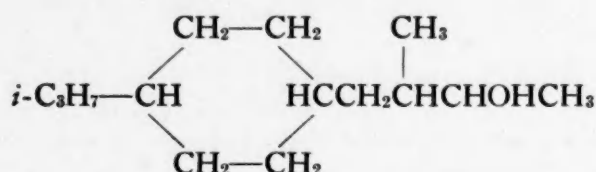
An illustration of this reaction is the acidic condensation of cuminaldehyde with methyl ethyl ketone. The condensation takes place on the methylene group,



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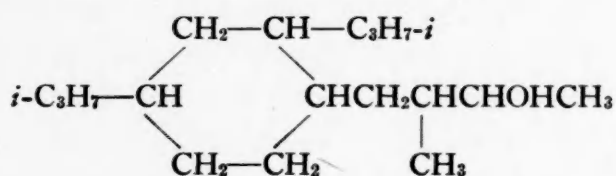
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whereas, with basic catalytic agents, the methyl group always reacts. The unsaturated ketone is next completely hydrogenated to 2-hydroxy-3-methyl-4-(4-isopropylcyclohexyl)-butane.



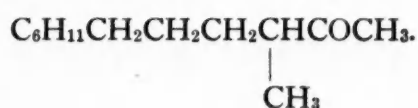
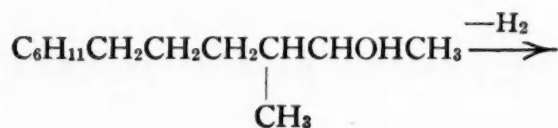
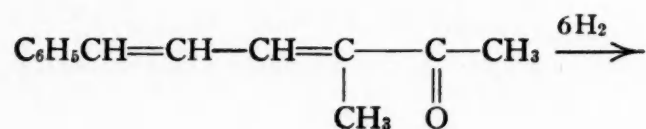
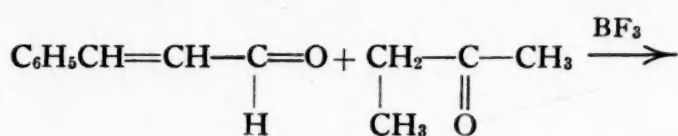
Upon dehydrogenating this alcohol, the ketone which is formed has the odor of East Indian sandalwood.

An interesting example of one of the effects of substitution in the benzene ring is shown by the alcohol, 2-hydroxy-3-methyl-4-(2,4-diisopropylcyclohexyl)-butane,



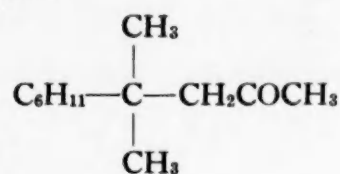
which has the odor of olibanum (frankincense). It is prepared from 2,4-diisopropylbenzaldehyde (obtained as a by-product in the preparation of cuminaldehyde), condensed with methyl ethyl ketone in a similar manner and reduced as before.

Lengthening the chain of the ketone seems to cause a reduction in the strength of the fragrance. The following outline shows the preparation of such a ketone, 2-keto-3-methyl-6-cyclohexylhexane:



The sandalwoodlike odor is less pronounced. It has not yet been determined how far this chain can be elongated and still retain a useful fragrance.

Branching of the chain causes a change in the fragrance. For example, the saturated ketone



has a fine and intense odor of vetiver oil. It is prepared by the addition of benzene to mesityl oxide, catalyzed by aluminum chloride. This results in a compound which, upon complete hydrogenation to the saturated alcohol and subsequent dehydrogenation, gives the fragrant saturated ketone.

The acidic catalyzed reaction which has been described above for the formation of the unsaturated ketones has been little used either in the laboratory or in industry, although it is apparently quite valuable. This reaction and several others used in the preparation of the fragrant substances are not complicated by any special techniques. They are straightforward and are easily handled in the plant. The use of these alcohols and their ketonic analogs in the perfume industry is also economically sound since most of the starting materials are not expensive.

A few of the structural variations which are responsible for differences of odor in these fragrant substances have been indicated; many others are immediately apparent. These may give added interest to the problem of new synthetics in the perfume industry.

Reference

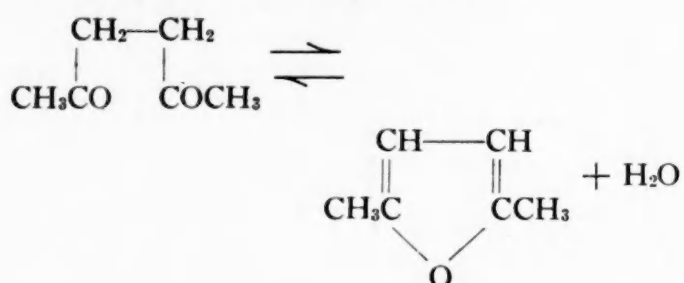
I. G. Farbenindustrie Research Reports: Wolfen Farben Works, 1942 No. 7, 1943 No. 4, as listed by R. L. Hasche in *Chem. Eng. News*, **23**, 1848 (October 25, 1945).

Microfilms of the complete reports in German are available as PB 839 and PB 846 from the Office of Technical Services, Department of Commerce, Washington, D. C.

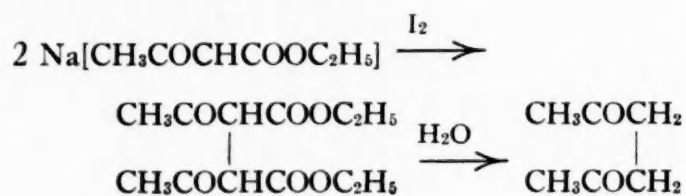
The Preparation of Saturated 1,4-Diketones

By C. F. H. ALLEN*

For many years a relatively small number of 1,4-diketones have been known. Acetylacetone, the first member of the series and the most accessible, is formed by a side reaction in the commercial catalytic oxidation of acetaldehyde to acetic acid. It is isolated as 2,5-dimethylfuran, which yields acetylacetone on acid hydrolysis.



In a more general type of reaction, it has been obtained by ketone hydrolysis of ethyl diacetosuccinate which, in turn, resulted from the coupling of two molecules of the sodium derivative of acetoacetic ester by iodine.

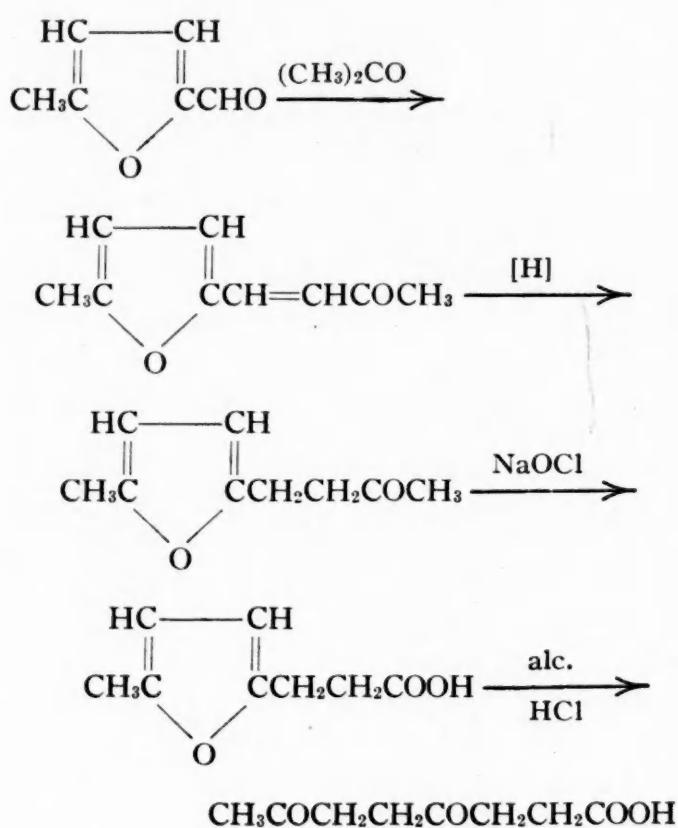


Since the yields in this reaction are very low and the manipulation is difficult, its usefulness is limited, and at present it is not employed to any extent. If it is attempted with higher homologs of acetoacetic ester in which the methyl group is alkylated, cyclopentenones result.

Largely through the work of Hunsdiecker, other methods for the preparation of saturated 1,4-diketones have been made practical. The four most useful of these will be described next.

The splitting of furans by acidic reagents appears to be of much more general utility than the acetoacetic ester method, owing to the cheapness of fur-

fural (5-methylfurfural, etc.), and its facile conversion to other substances that still retain the furan nucleus. For instance, 5-methylfurfural and acetone give 5-methylfurfuralacetone; the side-chain double bond can be selectively reduced, and the methyl ketone converted to an acid by means of sodium hypochlorite. The furan ring is cleaved by alcoholic hydrochloric acid, yielding acetyllevulinic acid. These reactions are summarized herewith.



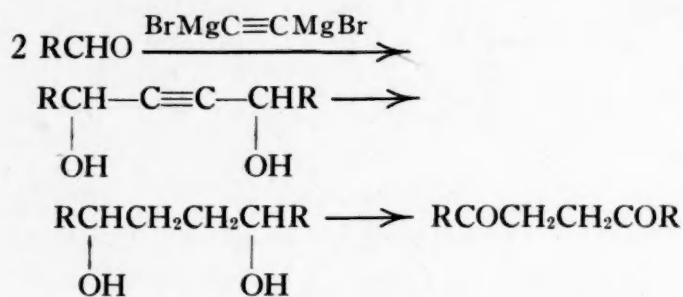
There are many obvious modifications; for example, the side-chain carbonyl group can be reduced to CH_2 , giving a methyl *n*-butylfuran. All these substances are important as sources of alkylated cyclopentenones.

Electrolysis of a mixture of acetyllevulinic acid and an aliphatic acid in methanol containing a trace of sodium methoxide gives three products from which the desired 1,4-diketone can be separated in a 30-45% yield by adequate fractionation. Thus, a mixture of acetyllevulinic and -caproic acids gives

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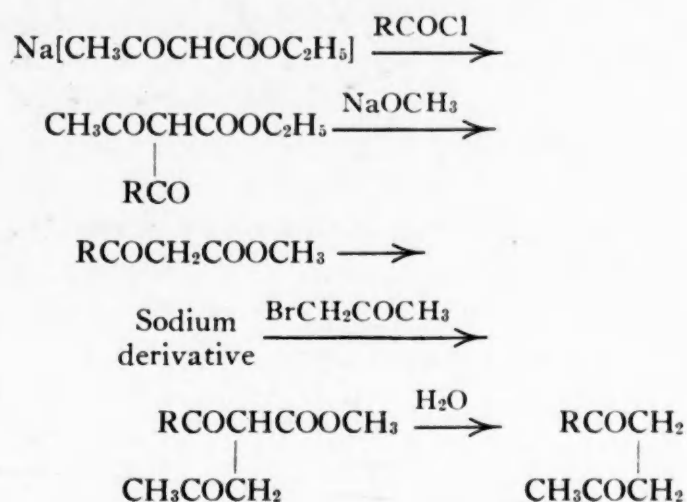
dodecan-2,5-dione, along with *n*-decane and tetradecan-2,5,10,13-tetrone. This method is limited in that only simple acids can be employed.

Dehydrogenation of secondary 1,4-diols also gives rise to 1,4-diketones. The diols are secured by a novel application of acetylene chemistry. It may be recalled that acetylenic Grignard reagents can be obtained, by treatment of acetylenes having at least one hydrogen left, by means of the cheap ethylmagnesium bromide. Thus, acetylene itself gives a "double reagent," $\text{BrMgC}\equiv\text{CMgBr}$. This reacts in normal fashion with carbonyl compounds to give acetylenic carbinols (diols). Upon catalytic reduction, the triple bond is reduced, and by means of suitable dehydrogenation catalysts, 1,4-diketones are formed.



Acid hydrolysis of α -acyllevulinic esters is another useful source of 1,4-diketones. This type of ester is readily secured by acylation of sodium acetoacetic ester, cleavage by sodium methoxide (in this step, the ethyl ester is changed to a methyl ester), and fractionation to isolate the acylacetic ester. The

latter, in the form of its sodium derivative, is then alkylated with bromoacetone to yield the desired product.



It should be noted that when unsymmetrical alkyl diketones are to be used for certain types of syntheses (e.g., cyclopentenones) there must be a CH_2 group in the R adjacent to the carbonyl group. Also if the hydrolysis is carried out in the presence of an alkaline reagent, the product is not the desired 1,4-diketone, but its cyclization product, a cyclopentenone; this reaction will form the subject of a subsequent article.

1,4-Diketones are used to obtain the heterocyclic systems of furan, thiophene, and pyrrole by well-known reactions found in all textbooks. The 1,4-diketones possess a very faint odor, much weaker than the corresponding monoketones having the same chain length. They should furnish suitable starting material for interesting investigations.

Some New Eastman Organic Chemicals

5856	4-Acetylamino-3-nitrobiphenyl MP 132-134° 100 g. . . \$ 7.00 C
	$\text{CH}_3\text{CONH}(\text{NO}_2)\text{C}_6\text{H}_3\text{C}_6\text{H}_5$. . . MW 256.25
2543	Cyclopentanone BP 129-132° 100 g. . . 4.50 C
	$\text{CH}_2(\text{CH}_2)_3\text{CO}$. . . MW 84.11
5818	6,9-Dichloro-2-methoxyacridine MP 162-164° 100 g. . . 5.00 C
	$\text{Cl}_2\text{C}_6\text{H}_2\text{CHC}_6\text{H}_3(\text{OCH}_3)\text{N}$. . . MW 278.13
5893	4,4'-Dimethoxystilbene MP 215-216° 100 g. . . 12.00 C
	$(\text{CH}_3\text{OC}_6\text{H}_4\text{CH})_2$. . . MW 240.29
5866	N-Ethylpiperidine (For Penicillin G Determination) 10 g. . . 2.00 A
	$\text{CH}_2(\text{CH}_2)_3\text{CH}_2\text{NC}_2\text{H}_5$. . . MW 113.20